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NEWS 19 APR 04 STN AnaVist, Version 1, to be discontinued
NEWS 20 APR 15 WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 21 APR 28 EMBASE Controlled Term thesaurus enhanced
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AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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=> s biotin
L1 95250 BIOTIN

=> s benzene
L2 399378 BENZENE

=> s aspartyl
L3 18645 ASPARTYL

=> s L1 and L2
L4 173 L1 AND L2

=> s L3 and L4
L5 0 L3 AND L4

=> s ethers or carboxylates or sulfonates or ammonium
L6 811867 ETHERS OR CARBOXYLATES OR SULFONATES OR AMMONIUM

=> s L4 and L6
L7 9 L4 AND L6

```
=> dup rem L7  
PROCESSING COMPLETED FOR L7  
L8          9 DUP REM L7 (0 DUPLICATES REMOVED)
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\Rightarrow d 1-9 1.8 ibib abs

L8 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:485496 CAPLUS
DOCUMENT NUMBER: 146:462680
TITLE: Water-soluble electropolymerizable monomers having
metalloporphyrin groups
INVENTOR(S): Canonne, Frederic; Korri, Youssoufi Hafsa; Mahy, Jean
Pierre; Mandrand, Bernard; Perree Fauvet, Martine
Biomerieux, Fr.; Centre National de la Recherche
Scientifique; Universite Paris Sud (Paris XI)
PATENT ASSIGNEE(S):
SOURCE: Fr. Demande, 57pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent

LANGUAGE : French

FAMILY ACC. NUM. COUNT: 1

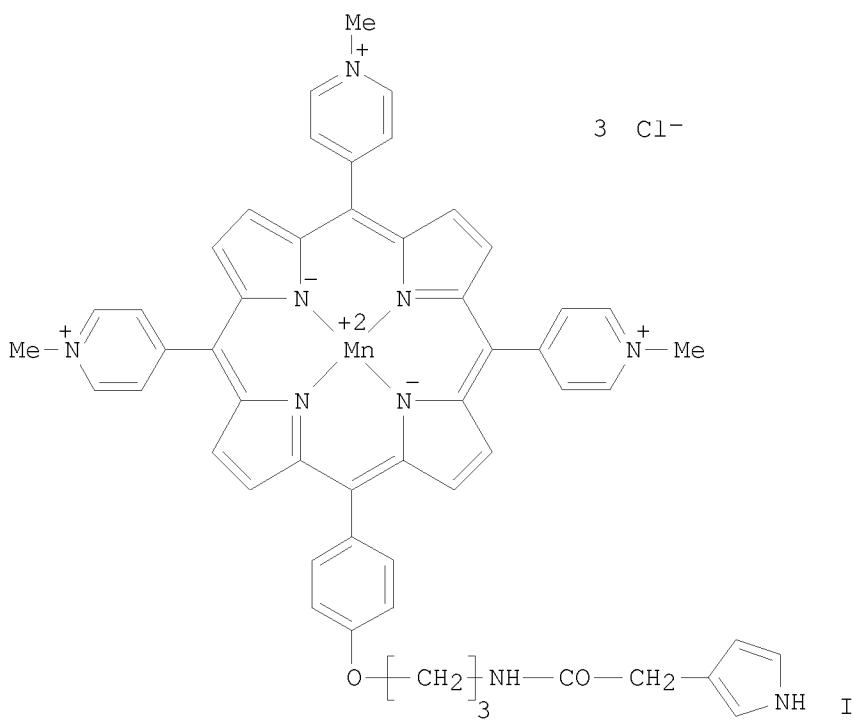
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2892723	A1	20070504	FR 2005-11187	20051103
WO 2007051947	A1	20070510	WO 2006-FR51131	20061102
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: FR 2005-11187 A 20051103

OTHER SOURCE(S): MARPAT 146:462680

GI



AB Metallocporphyrins are manufactured having electropolymerizable groups and ≥ 2 groups that are ionizable or ionized in water. Thus, reaction of 4-hydroxybenzaldehyde with N-(3-bromopropyl)phthalimide, cyclization of the intermediate with 4-pyridinecarboxaldehyde and pyrrole, hydrolysis of the resulting porphyrin derivative, reaction of the resulting porphyrin derivative having a 3-aminoproxy group with 1H-pyrrol-3-ylacetic acid, methylation

of the resulting porphyrin derivative having an amide group, and metalation of the resulting porphyrin deriv salt with Mn gave a complex I, which exhibited electropolymerizability.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1270480 CAPLUS
DOCUMENT NUMBER: 147:507931
TITLE: Procedure for the biodegradation of MTBE AND TBA in the presence of additional organic pollutants by means of carrier-fixed microorganisms
INVENTOR(S): Rohwerder, Thore; Mueller, Roland H.; Martienssen, Marion
PATENT ASSIGNEE(S): Ufz-Umweltforschungszentrum Leipzig-Halle G.m.b.H., Germany
SOURCE: Ger. Offen., 8pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102006022042	A1	20071108	DE 2006-102006022042	20060505
PRIORITY APPLN. INFO.:			DE 2006-102006022042	20060505

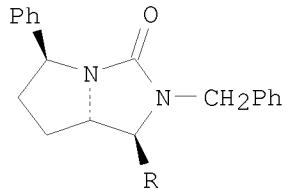
AB The invention concerns a procedure for the biol. degradation of Me tert. Bu ether (MTBE) and/or tert-Bu alc. (TBA), optionally in presence of further pollutants from contaminated waters. In addition to MTBE and TBA, BTEX compds. (benzene, toluene, ethylbenzene, xylene) as well as petroleum mineral oil hydrocarbons can be simultaneously eliminated. The invention concerns a bacterial strain specialized for the complete mineralization of MTBE, Ideonella sp. L-108, , which is settled on a substrate, used for the biodegrdn. of the contaminant(s). The characteristics of the carrier are specifically optimized for the settlement of these bacteria. According to the invention substrates with a moderately hydrophobic character, without or with weakly cationic net charge, are preferable, including burned clay granulate, lava tuff and polystyrene.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:907178 CAPLUS
DOCUMENT NUMBER: 146:337875
TITLE: A process for the preparation of substituted 6-benzyl-5-oxo-3-phenyl-(3S,7S,7aR)-perhydroimidazo[1,5-c][1,3]thiazoles
INVENTOR(S): Chavan, Subhash Prataprao; Gopal, Chittiboyina Amar; Kamat, Subhash Krishnaji; Kalkote, Uttam Ramrao; Ravindranathan, Thotapallil
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research, India
SOURCE: Indian, 17pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

IN 194355 A1 20041023 IN 2001-DE302 20010319
 US 6486328 B1 20021126 US 2000-686908 20001012
 PRIORITY APPLN. INFO.: US 2000-686908 A 20001012
 OTHER SOURCE(S): CASREACT 146:337875; MARPAT 146:337875
 GI



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AB A process for the preparation of substituted 6-benzyl-5-oxo-3-phenyl-(3S,7S,7aR)-perhydroimidazo[1,5-c][1,3]thiazoles having general formula I [R = 1-phenyl-1-ethanone, 1-(4-chlorophenyl)-1-ethanone, 1-(4-methoxyphenyl)-1-ethanone, 2-oxocyclohexyl, 1-trimethylsilyloxy-2-oxocyclohexyl, allyl, 1-hexynyl, 4-dimethyl aminophenyl, or 2-methylpropanoate] which comprises reacting the compound 6-benzyl-7-hydroxy-3-phenyl-(3S,7aR)-perhydroimidazol[1,5-C][1,3]thiazol-5-one as described herein with Lewis acid and a nucleophile at a temperature ranging between 0 to 30°C in an organic solvent for 10-30 min, quenching the reaction mixture with quenching agent (preferably with water and/or saturated aqueous solution of salts of sodium, potassium, ammonium), separating and concentrating the organic layer, and purifying by known conventional methods such as chromatog. (silica gel) to obtain I. I have the potential as serving as intermediates to biotin or as chiral auxiliaries.

L8 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:525055 CAPLUS
 DOCUMENT NUMBER: 141:76350
 TITLE: Oxidative hair dyes containing derivatives of indoline, p-phenylene diamine and conditioners
 INVENTOR(S): Kleen, Astrid
 PATENT ASSIGNEE(S): Henkel Kommanditgesellschaft Auf Aktien, Germany
 SOURCE: Eur. Pat. Appl., 24 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1433470	A1	20040630	EP 2003-29369	20031219
EP 1433470	B1	20080326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
DE 10260835	A1	20040701	DE 2002-10260835	20021223
AT 390118	T	20080415	AT 2003-29369	20031219
PRIORITY APPLN. INFO.:			DE 2002-10260835	A 20021223

OTHER SOURCE(S): MARPAT 141:76350

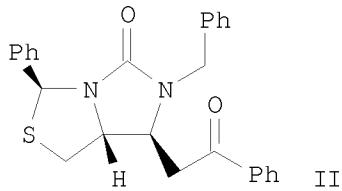
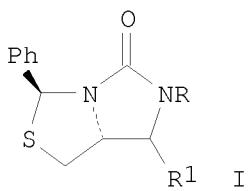
AB The invention concerns oxidative hair dyes that contain in a cosmetically acceptable carrier (a) at least one indoline derivative; (b) at least one p-phenylene diamine derivative; (c) hair care substances selected from the group of (c1) vitamins and provitamins, e.g. vitamins A, B, E and H; (c2) ectoin and its derivs., allantoin and bisabolol. Addnl. developers and cationic direct dyes can be added. Thus a hair dye cream contained

(weight/weight%): Texapon NSO 15; Dehyton K 12; Lorol 4; Hydrenol 10; Eumulgin B1 0.5; Eumulgin B2 0.5; ascorbic acid 0.5; sodium sulfite 0.5; ammonium hydrogenphosphate 1; ammonia to pH10; 1-(2-hydroxyethyl)-2,5-diaminobenzene sulfate 1.3; 5,6-dihydroxyindoline hydrobromide 0.1; 2-methylresorcin 0.09; 4-chlororesorcin 0.3; m-aminophenol 0.05; 2,7-dihydroxynaphthalene 0.23; 2,4,5,6-tetraaminopyrimidine 0.03; 1-methoxy-2-amino-4-(2-hydroxyethylamino)benzene sulfate 0.03; Vitamin B6 0.5; water to 100.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2002:503386 CAPLUS
 DOCUMENT NUMBER: 137:63120
 TITLE: Process for preparing perhydroimidazol[1,5-c][1,3]thiazol-5-one derivatives as intermediates for synthesis of D(+) -biotin
 INVENTOR(S): Chavan, Subhash Prataprao; Chittiboyina, Amar Gopal; Kamat, Subhash Krishnaji; Kalkote, Uttam Ramrao; Ravindranathan, Thotapallil
 PATENT ASSIGNEE(S): Council of Scientific and Industrial Research, India
 SOURCE: Eur. Pat. Appl., 14 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1219625	A1	20020703	EP 2000-128571	20001227
EP 1219625	B1	20060517		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 326471	T	20060615	AT 2000-128571	20001227
PT 1219625	T	20061031	PT 2000-128571	20001227
ES 2264919	T3	20070201	ES 2000-128571	20001227
PRIORITY APPLN. INFO.:			EP 2000-128571	A 20001227
OTHER SOURCE(S):	CASREACT 137:63120; MARPAT 137:63120			
GI				



AB The present invention discloses a process for preparing substituted perhydroimidazol[1,5-c][1,3]thiazol compds., such as I [R = benzyl; R1 = alkyl group exemplified by 1-phenyl-1-ethanone, 1-(4-chlorophenyl)-1-ethanone, α -(4-methoxyphenyl)-1-ethanone, 2-oxocyclohexyl, 1-trimethylsilyloxy-2-oxocyclohexyl, allyl, 1-hexanyl, etc.], as crucial intermediates for the synthesis of D(+) -biotin. Thus, D(+) -biotin intermediate II was prepared by the reaction of 1-trimethylsilyloxystylene and 6-benzyl-7-hydroxy-3-phenyl-(3S,7aR)-perhydroimidazol[1,5-c][1,3]thiazol-5-one in presence of boron trifluoride etherate. These compds. are more stable and are produced by non-hazardous

methods.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:861452 CAPLUS
DOCUMENT NUMBER: 134:29252
TITLE: Synthesis of water soluble multi-biotin-containing compounds for use in targeting biotin-binding proteins
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
WO 2000072802	A2	20001207	WO 2000-US15081	20000601
WO 2000072802	A3	20020207		
		W: AU, BR, CA, IL, JP, KR, MX, RU		
		RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE		
EP 1196199	A2	20020417	EP 2000-938025	20000601
		R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		

PRIORITY APPLN. INFO.: US 1999-324267 A 19990602
WO 2000-US15081 W 20000601

AB Syntheses of water soluble discrete multi-biotin-containing compds. with at least three biotin moieties are disclosed. The water soluble biotin-containing compds. may addnl. comprise one or more moieties that confer resistance to cleavage by biotinidase or that is cleavable in vitro or in vivo. The discrete multi-biotin-containing compds. may include a reactive moiety that provides a site for reaction with yet another moiety, such as a targeting, diagnostic or therapeutic functional moiety. Biotinylation reagents comprising water soluble linker moieties are also disclosed and may addnl. comprise a biotinidase protective group. Methods for amplifying the number of sites for binding biotin-binding proteins at a selected target using multi-biotin compds. are also disclosed.

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:784331 CAPLUS
DOCUMENT NUMBER: 132:20747
TITLE: Surface regeneration of biosensors using a combination of solutions based on interaction-specific optimized processes
INVENTOR(S): Andersson, Karl; Hamalainen, Markku; Malmqvist, Magnus; Roos, Hakan
PATENT ASSIGNEE(S): Biacore AB, Swed.
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
WO 9963333	A1	19991209	WO 1999-SE921	19990531

W: AU, JP, US
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE
 US 6289286 B1 20010911 US 1998-87402 19980529
 AU 9946658 A 19991220 AU 1999-46658 19990531
 AU 755181 B2 20021205
 EP 1082607 A1 20010314 EP 1999-930044 19990531
 R: BE, CH, DE, FR, GB, LI, NL, SE, FI
 JP 2002517720 T 20020618 JP 2000-552490 19990531
 PRIORITY APPLN. INFO.: US 1998-87402 A 19980529
 WO 1999-SE921 W 19990531

AB Surface regeneration of affinity biosensors and characterization of biomols. associated therewith by multivariate technique employing cocktails of regeneration agents to optimize regeneration of biosensor surface and/or characterize biomols. associated therewith. Kits and stock solns. for use in the context of this invention, as well as associated computer algorithms are also disclosed. Stock solns. of regeneration cocktails are prepared and combined. Solns. are acidic, basic, ionic, organic, detergent and chelating agent containing Biosensors for various affinity bindings are regenerated by the method; the affinity reactions are used for optimizing the regeneration process. Immuno-reactions, nucleic acid hybridization, avidin/streptavidin-biotin, hormone-hormone receptor interactions are performed with Biocore instruments and CM5 sensor chips.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1966:11410 CAPLUS
 DOCUMENT NUMBER: 64:11410
 ORIGINAL REFERENCE NO.: 64:2057h,2058a-b
 TITLE: Substituted indole derivatives
 INVENTOR(S): Shavel, John, Jr.; Strandtmann, Maximilian Von
 PATENT ASSIGNEE(S): Warner-Lambert Pharmaceutical Co.
 SOURCE: 2 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
US 3217029		19651109	US 1961-119830	19610627

PRIORITY APPLN. INFO.:

AB A solution of 40 g. p-H₂NC₆H₄COMe in 250 ml. H₂O and 143 ml. concentrated HCl was

added at 0-5° dropwise and with stirring to a solution of 21 g. NaNO₂ in 200 ml. H₂O. To the resulting solution was added 60.3 g. ethyl α-(2-dimethylaminoethyl)acetooacetate and 63 g. NaOAc. The mixture was maintained at pH 6-7 with 3N NaOH, stirred in the cold 2 hrs., basified, and extracted with CHCl₃ to yield 65 g. ethyl α-oxo-γ-dimethylaminobutyrate p-acetylphenylhydrazone (I), m. 78-80° (petr.-ether). A mixture of 43 g. I and 430 g. polyphosphoric acid was heated with stirring at 100-110° for 2 hrs., poured into ice-H₂O, basified with 3N NaOH, and extracted with 400 ml. CHCl₃. The residue from the CHCl₃ solution was dissolved in EtOAc and treated with ethereal HCl to yield 17.8 g. 5-acetyl-2-carbethoxygramine-HCl, m. 211-14° (MeCN). These compds. lower blood pressure, increase coronary flow, exhibit anti-serotonin activity, and depress the central nervous system.

L8 ANSWER 9 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 1949:21300 BIOSIS

DOCUMENT NUMBER: PREV19492300021501; BA23:21501

TITLE: Glutinosin. A fungistatic metabolic product of the mould Metarrhizium glutinosum S. Pope.
AUTHOR(S): BRIAN, P. W.; CURTIS, P. J.; HEMMING, H. G.
CORPORATE SOURCE: Butterwick Re. Labs., Welwyn, Herts, Eng.
SOURCE: PROC ROY SOC SER B BIOL SCI, (1947) Vol. 135, No. 878, pp. 106-132.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable
ENTRY DATE: Entered STN: May 2007
Last Updated on STN: May 2007

AB When *M. glutinosum* is grown at pH 3.6 on Raulin-Thom medium, the glutinosin content reaches a peak of 256 B.A. U./ml. as measured by the inhibition of germination of *Botrytis allii* conidia. Bacteriostatic action against *Staphylococcus aureus* or *Salmonella typhi* is minimal. Biotin and aneurin supplements produce marked stimulation of sporulation and slight increase in glutinosin production. Nitrate stimulates growth but not glutinosin production. Inorganic ammonium salts are ineffective for growth or glutinosin production, but peptone or the addition of 0.1-1% of tartaric, malic, succinic, malonic, oxalic, citric, acetic, glycollic, pyruvic, aspartic or glutamic acids to a medium containing 0.16% (NH₄)₂SO₄, 5% dextrose, and minerals, is highly effective in promoting growth and glutinosin production, pointing to a need for intermediates of the Krebs cycle for effective utilization of carbohydrate when the ammonia path of assimilation is followed. Cultures with the monocarboxylic acids were at initial pH 6.5 to lessen the toxicity of the free acid, but cultures with the dicarboxylic acids were started at pH 4. Glutinosin was extracted from culture medium by petroleum ether to yield on evaporation a gummy crystalline mass, which recrystallized from ethanol as a white microcrystalline solid, glutinosin, C₄₈H₆₀O₁₆. For routine production, a solution containing 50 g. glucose, 0.75 g. H₃PO₄, 10 g. malic acid, 0.5 g. MgSO₄, and 1 ml. minor element concentrate in 1 liter adjusted to pH 4 with a solution that is 2.5 N with respect to both KOH and NH₄OH, yields 100 mg. glutinosin when the glutinosin is absorbed on 10 g. charcoal and extracted 6 hrs. with benzene in a Soxhlet extractor. Aqueous solns. of glutinosin are relatively stable at pH 3, with 50% activity loss in 9 days at 25[degree]C or on autoclaving 20 min. at 15 lbs. Toxicity data are given for 34 fungi and 10 bacteria. *M. glutinosum* cultures produce a volatile, water-soluble dermatitic substance, so that ventilation and barrier creams must be used when working with culture filtrates. ABSTRACT AUTHORS: E. H. Shaw, Jr

=> s trifunctional
L9 5853 TRIFUNCTIONAL

=> s L1 and L9
L10 88 L1 AND L9

=> s asparty1
L11 18645 ASPARTYL

=> s L10 and L11
L12 1 L10 AND L11

=> d L12 ibib abs

L12 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:583437 BIOSIS
DOCUMENT NUMBER: PREV200200583437
TITLE: Trifunctional conjugation reagents. Reagents that

contain a biotin and a radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies.

AUTHOR(S): Wilbur, D. Scott [Reprint author]; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.; Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin

CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, 2121 N. 35th Street, Seattle, WA, 98103-9103, USA
dswilbur@u.washington.edu

SOURCE: Bioconjugate Chemistry, (September-October, 2002) Vol. 13, No. 5, pp. 1079-1092. print.
CODEN: BCCHE. ISSN: 1043-1802.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002

AB A method of removing radiolabeled monoclonal antibodies (mAbs) from blood using a device external to the body, termed extracorporeal affinity-adsorption (EAA), is being evaluated as a means of decreasing irradiation of noncancerous tissues in therapy protocols. The EAA device uses an avidin column to capture biotinylated-radiolabeled mAbs from circulated blood. In this investigation, three trifunctional reagents have been developed to minimize the potential deleterious effect on antigen binding brought about by the combination of radiolabeling and biotinylation of mAbs required in the EAA approach. The studies focused on radiolabeling with ^{111}In and ^{90}Y , so the chelates CHX-A"-DTPA and DOTA, which form stable attachments to these radionuclides, were incorporated in the trifunctional reagents. The first trifunctional reagent prepared did not incorporate a group to block the biotin cleaving enzyme biotinidase, but the two subsequent reagents coupled aspartic acid to the biotin carboxylate for that purpose. All three reagents used 4,7,10-trioxa-1,13-tridecanediamine as water-soluble spacers between an aminoisophthalate core and the biotin or chelation group. The mAb conjugates were radioiodinated to evaluate cell binding as a function of substitution. Radioiodination was used so that a direct comparison with unmodified mAb could be made. Evaluation of the number of conjugates per antibody versus cell binding immunoreactivities indicated that minimizing the number of conjugates was best. Interestingly, a decrease of radioiodination yield as a function of the number of isothiocyanate containing conjugates per mAb was noted. The decreased yields were presumably due to the presence of thiourea functionality formed in the conjugation reaction. Radiolabeling with ^{111}In and ^{90}Y was facile at room temperature for conjugates containing the CHX-A", but elevated temperature (e.g., 45degreeC) was required to obtain good yields with the DOTA chelate. Stability of ^{90}Y labeled mAb in serum, and when challenged with 10 mM EDTA, was high. However, challenging the ^{90}Y labeled mAb with 10 mM DTPA demonstrated high stability for the DOTA containing conjugate, but low stability for the CHX-A" containing conjugate. Thus, the choice between these two chelating moieties might be made on requirements for facile and gentle labeling versus very high in vivo stability. Application of the trifunctional biotinylation reagents to the blood clearance of labeled antibodies in EAA is under investigation. The new reagents may also be useful for other applications.

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FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
55.42	55.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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